

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

MacLEAN et al

Serial No. 08/776,350

Filed: April 18, 1997

Title: TREATMENT OF CANCER USING HSV MUTANT

Assistant Commissioner for Patents
Washington, DC 20231

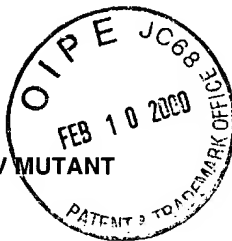
Atty Dkt. 620-73

C#/M#

Group Art Unit: 1642

Examiner: Unger

Date: February 10, 2000



Sir:

SUPPLEMENTAL SUBMISSION

This is a response/amendment/letter in the above-identified application and includes an attachment which is hereby incorporated by reference and the signature below serves as the signature to the attachment in the absence of any other signature thereon.

Fees are attached as calculated below:

Total effective claims after amendment	0	minus highest number		
previously paid for	20	(at least 20) =	0 x \$ 18.00	\$ 0.00
Independent claims after amendment	0	minus highest number		
previously paid for	3	(at least 3) =	0 x \$ 78.00	\$ 0.00
If proper multiple dependent claims now added for first time, add \$260.00 (ignore improper)				\$ 0.00
Petition is hereby made to extend the current due date so as to cover the filing date of this paper and attachment(s) (\$110.00 /1 month; \$380.00/2 months; \$870.00/3 months)				\$ 0.00
Terminal disclaimer enclosed, add \$110.00				\$ 0.00
First submission after Final Rejection pursuant to 37 CFR 1.129(a) (\$690.00)				\$ 0.00
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The Commissioner is hereby authorized to charge any deficiency in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our **Account No. 14-1140**. A duplicate copy of this sheet is attached.

1100 North Glebe Road
8th Floor
Arlington, Virginia 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100
BJS:rdw

NIXON & VANDERHYE P.C.

By Atty: B.J. Sadoff, Reg. No. 36,663

Signature: _____

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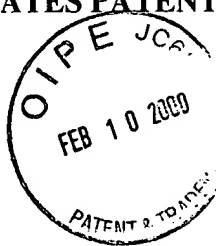
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Examiner: S. Unger

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February 10, 2000

Assistant Commissioner of Patents
Washington, DC 20231

Sir:

SUPPLEMENTAL SUBMISSION

Supplemental to the Amendment of December 30, 1999, the applicants note, for completeness, that gliomas were incorrectly identified as being benign on page 6, penultimate line, of the Amendment. While it is true that gliomas are not "metastatic", such that they would not be included as a tumor to be treated by the presently claimed method, gliomas are not "benign". More specifically, gliomas are malignant while not being metastatic. See, the attached pages 162 and 771 of Dorland's Illustrated Medical Dictionary (26th Edition) 1981 W.B. Saunders Company, Philadelphia, PA.

One of ordinary skill in the art would appreciate that gliomas are tumors that are produced in the brain from glial cells which are the normal supporting cells in the brain and that they are tumors which are restricted to the brain. Gliomas are not classified as metastatic tumors as they do not metastasize to other sites of the body. Upon removal by surgery, gliomas regrow

again in the brain and do not spread beyond the brain. Gliomas are characterized by over expression of glial fibrillary acidic protein (GFAP), which is a normal marker of glial cells. The over expression of GFAP is known as a characteristic of gliomas and changes which take place to transform normal glial cells into tumor cells are known to be contained entirely within the central nervous system and not elsewhere in the body.

Metastatic tumors, on the other hand, can arise from virtually all other types of malignant tumors in organs other than the brain. That is, metastatic tumors from the breast, lung, bowel, etc., can metastasize to other vital organs, including the brain. For instance, it is common for breast tumors and melanomas to metastasize to the brain. Metastasis is, therefore, a generalized process, usually with multiple foci of metastases, arising from a single primary tumor at an unrelated site. Sometimes, cancer is only diagnosed when a metastasized tumor produces problems. Metastatic cancer cells have the capacity to spread throughout the body and this is quite different from glioma cells which are entirely restricted to the brain.

One of ordinary skill would also appreciate that the cell markers of tumors are different and depend from the origin of the tumor. Metastasized tumors will have different expression patterns and different pathology, depending on the pathology of the primary tumor. Gliomas will always have the same pathology and the same markers. In other words, when a brain tumor is diagnosed on a scan and a biopsy is taken for pathology, there is an unambiguous distinction between a glioma and metastatic brain tumor arising from, for example, a primary breast tumor.

Accordingly, gliomas are not within the scope of tumors treated by the presently claimed method and the inadvertent error in referring to gliomas as "benign" is regretted.

An early and favorable Action on the merits is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____



B.J. Sadoff
Reg. No. 36,663

BJS:rdw
1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4091
Facsimile: (703) 816-4100

- gastric muscle**, venter anterior muscoli digastrici. **delhi b.**, a dysenteric infection occurring in tropical countries, manifested as an acute diarrheal disease. **drum b.**, tympanic abdomen. **frontal b. of occipitofrontal muscle**, venter occipitalis muscoli occipitofrontalis. **occipital b. of occipitofrontal muscle**, venter occipitalis muscoli occipitofrontalis. **posterior b. of digastric muscle**, venter posterior muscoli digastrici. **prune b.**, see under *syndrome*. **swollen b.**, tympanites in animals. **wooden b.**, abdominal rigidity.
- belonoid** (bel'o-noid) [Gr. *belonē* needle + *eidos* form] needle-shaped; styloid.
- belonoskiacopy** (bel'o-no-ski-as/ko-pe) [Gr. *belonē* needle + *skia* shadow + *skopein* to examine] a method of retinoscopy.
- beloxamide** (bel-oks'ah-mid) chemical name: *N*-(benzyloxy)-*N*-(3-phenylpropyl)acetamide; an anticholesteremic agent, $C_{18}H_{21}NO_2$.
- belt** (belt) an encircling band worn about the waist or abdomen; called also *balteum*. Cf. *girdle*.
- bemegride** (bem'ē-grid) chemical name: 4-ethyl-4-methyl-2,6-piperidinedione. An analeptic drug, $C_8H_{13}NO_2$, which has been used in the treatment of barbiturate poisoning.
- bemidone** (bem'i-dōn) chemical name: ethyl 4-(*m*-hydroxyphenyl)-1-methylisonipicotate. A crystal compound, $C_{13}H_{17}NO_3$, soluble in water; formerly used as a narcotic and analgesic.
- benactyzine hydrochloride** (ben-ak'ti-zēn) chemical name: α -hydroxy- α -phenylbenzeneacetic acid 2-(diethylamino)ethyl ester hydrochloride. An anticholinergic, $C_{20}H_{25}ClNO_3$, occurring as a white, crystalline powder, which has the ability to increase the emotional threshold of outside influences and to block the thought processes; used as a tranquilizer, administered orally.
- Benadryl** (ben'ah-dril) trademark for preparations of diphenhydramine hydrochloride.
- benapryzine hydrochloride** (ben-ah-pri'zēn) chemical name: 2(ethylpropylamino)ethyl benzilate hydrochloride; an anticholinergic, $C_{21}H_{27}NO_3 \cdot HCl$.
- Bence Jones protein**, etc. [Henry Bence Jones, English physician, 1814-1873] see under *cylinder*, *protein*, *proteinuria*, and *reaction*.
- bend** (bend) a flexure or curve; a flexed or curved part. **first order b's**, adjustments made in a labial arch wire, incorporating offsets in the horizontal plane, which are usually made in the areas of the cuspids and premolar and molar teeth, accommodating differences in thickness in the labiolingual or buccolingual diameters of the teeth. **head b.**, cephalic flexure. **neck b.**, cervical flexure. **second order b's**, bends in the vertical plane of an arch wire. **third order b's**, bends in an arch wire to maintain or produce torsion of a tooth. **V b's**, V-shaped bends incorporated in an arch wire, usually placed mesial or distal to the cuspids to improve the axial relationship of teeth. **varolian b.**, the third cerebral flexure in the developing fetus.
- bendazac** (ben'dah-zak) chemical name: [(1-benzyl-1*H*-indazol-3-yl)oxy]acetic acid; an anti-inflammatory agent, $C_{18}H_{17}N_3O_3$.
- Bendectin** (ben-dek'tin) trademark for tablets containing a combination of dicyclomine hydrochloride, doxylamine succinate, and pyridoxine hydrochloride; used in management of nausea and vomiting during pregnancy.
- bendroflumethiazide** (ben'dro-floo'ah-zid) bendroflumethiazide.
- bendroflumethiazide** (ben'dro-floo'mē-thi'ah-zid) [USP] chemical name: 3,4-dihydro-3-(phenylmethyl)-6-(trifluoromethyl)-2*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide. A white to cream-colored crystalline powder, $C_{15}H_{11}F_3N_3O_4S_2$, used as an oral diuretic and antihypertensive.
- bends** (bendz) pain in the limbs and abdomen occurring as a result of rapid reduction of air pressure; see *decompression sickness*, under *sickness*.
- Bendylate** (ben'di-lāt) trademark for preparations of diphenhydramine hydrochloride.
- bene** (be'ne) [L.] well.
- beneceptor** (ben'e-sep-tor) [L. *bene* well + *ceptor*] a rarely used term for a receptor that transmits stimuli of a beneficial character. Cf. *nociceptor* and *ceptor*, def. 2.
- Beneckea** (be-nek'e-ah) a genus of microorganisms of the family Achromobacteraceae, order Eubacteriales, made up of small to medium-sized rods, found in salt and fresh water and soil, which may or may not be chromogenic. It includes six species, *B. chittino'vora*, *B. hyperop'tica*, *B. indolhe'tica*, *B. la'bra*, *B. lipo'phaga*, and *B. ureaso'phora*.
- Benedict's test** (ben'e-dikts) [Stanley Rossiter Benedict, American physiological chemist, 1884-1936] see under *tests*.
- Benedict-Hopkins-Cole reagent** (ben'ē-dikt-hop/kinz-kōl) [Stanley Rossiter Benedict; Sir Frederick Gowland Hopkins, English biologist, 1861-1947; Sidney William Cole, English physiologist, born 1877] see under *reagent*.
- Benedikt's syndrome** (ben'e-dikts) [Moritz Benedikt, Austrian physician, 1835-1920] see under *syndrome*.
- benign** (be-nin') [L. *benignus*] not malignant; not recurrent; favorable for recovery.
- benignant** (be-nig'nant) benign.
- Béniqué's sound** (ba-ne-kāz') [Pierre Jules Béniqué, French physician, 1806-1851] see under *sound*.
- Benisone** (ben'i-sōn) trademark for preparations of betamethasone benzoate.
- benjamin** (ben'jah-min) benzoin, def. 1.
- Bennet's corpuscles** (ben'ets) [James Henry Bennet, English obstetrician, 1816-1891] see *Nunn's gorged corpuscles* and *Drysdale's corpuscles*, under *corpuscle*.
- Bennett's disease** (ben'ets) [John Hughes Bennett, English physician, 1812-1875] leukemia.
- Bennett's fracture, operation** (ben'ets) [Edward Hallaran Bennett, Irish surgeon, 1837-1907] see under *fracture* and *operation*.
- Benoquin** (ben'o-kwin) trademark for preparations of monobenzone.
- benorterone** (bē-nor'ter-ōn) chemical name: 17 β -17-hydroxy-17-methyl-B-norandrost-4-en-3-one; an antiandrogen, $C_{24}H_{36}O_2$.
- benoxaprofen** (ben-oks'ah-pro'fen) chemical name: 2-(4-chlorophenyl)- α -methyl-5-benzoxazoleacetic acid; an anti-inflammatory and analgesic, $C_{18}H_{15}ClNO_3$.
- benoxinate hydrochloride** (ben-ok'si-nāt) [USP] chemical name: 4-amino-3-butoxybenzoic acid 2-(diethylamino)ethyl ester monohydrochloride. A local anesthetic, $C_{17}H_{25}N_2O_4 \cdot HCl$, occurring as white crystals or as a white, crystalline powder; used in ophthalmology, applied topically to the conjunctiva.
- Benoxyl** (ben-ok'sil) trademark for preparations of benzoyl peroxide.
- benserazide** (ben-ser'ah-zid) chemical name: 2-[(2,3,4-trihydroxyphenyl)-methyl]hydrazide DL-serine; a decarboxylase inhibitor, $C_{10}H_{15}N_3O_5$.
- Benson's disease** (ben'sunz) [Alfred Hugh Benson, Irish ophthalmologist, 1852-1912] asteroid hyalosis.
- benzazepam** (ben-taz'ē-pam) chemical name: 1,3,6,7,8,9-hexahydro-5-phenyl-2*H*-[1]benzothieno[2,3-*e*]-1,4-diazepin-2-one; a tranquilizer, $C_{17}H_{14}N_2OS$.
- benthos** (ben'thos) [Gr. *benthos* bottom of the sea] the flora and fauna of the bottom of oceans.
- bentonite** (ben'ton-it) [NF] a native, colloidal, hydrated aluminum silicate, which on the addition of water swells to produce a slippery paste; its chief pharmaceutical use is as a suspending agent, and it has also been used as a bulk laxative.
- Bentyl** (ben'til) trademark for preparations of dicyclomine hydrochloride.
- benzaldehyde** (ben-zal'dē-hid) [NF] artificial essential oil of almond; used as a flavoring agent in orally administered medications.
- benzalin** (ben'zah-lin) nigrosin.
- benzalkonium chloride** (ben'zal-ko'ne-um) [NF] a mixture of alkylbenzyl dimethylammonium chlorides of the general formula, $[C_6H_5CH_2N(CH_3)_2R]Cl$. A rapidly acting surface disinfectant and detergent, occurring as a white or yellowish white, thick gel or gelatinous pieces, which is active against both gram-negative and gram-positive bacteria and certain viruses, fungi, yeasts, and protozoa; applied topically to the skin and mucous membranes. It is also used as an antimicrobial preservative in ophthalmic solution.
- benzamidase** (ben-zam'i-dās) an enzyme that catalyzes the change of benzoic acid into benzamide.
- benzamine** (ben'zah-mēn) eucaine.
- benzanthracycline** (ben-zan'thrāh-sēn) one of a group of hydrocarbons some of which have carcinogenic properties.
- benzazoline hydrochloride** (benz-az'o-lēn) tolazoline hydrochloride.
- benzbromarone** (benz-bro'mah-rōn) chemical name: (3,5-dibromo-4-hydroxyphenyl)-(2-ethyl-3-benzofuranyl)methanone; uricosuric drug, $C_{17}H_{12}Br_2O_3$.
- benzcurine iodide** (benz'ku-rēn) gallamine triethiodide.
- Benzedrex** (ben'zē-dreks) trademark for a propylhexedrine inhaler.
- Benzedrine** (ben'zē-drēn) trademark for preparations of amphetamine sulfate.
- benzene** (ben'zēn) a colorless volatile liquid hydrocarbon, C_6H_6 , obtained mainly as a by-product in the destructive distillation of coal, along with coal tar, etc. It has an aromatic odor, and burns with a light-giving flame. It dissolves sulfur, phosphorus, iodine, and organic compounds. The fumes may cause fatal poisoning. It was formerly used as a pulmonary antiseptic in influenza, etc., as a teniacide, externally as a parasiticide, and has been suggested for leukemias. Called also *benzol*. **dimethyl b.**, xylene. **hexachloride**, chemical name: 1,2,3,4,5,6-hexachlorocyclohexane. A compound, $C_6H_2Cl_6$, prepared by chlorination of benzene. Certain liquids consisting of five isomers, the gamma isomer being

-cic (mah-la'sik) marked by malacia or morbid softness.
co- [Gr. *malakos* soft] a combining form meaning a condition of abnormal softness.
coma (mal'ah-ko'mah) [*malaco-* + *-oma*] a morbidly soft state or spot.
coplaxia (mal'ah-ko-pla'ke-ah) [*malaco-* + Gr. *plax* plaque] formation of soft patches on the mucous membrane of a hollow organ.
m. vesicae, a soft, yellowish, fungus-like growth on mucous membrane of the bladder and ureters.
cosarcosis (mal'ah-ko-sar-ko'sis) [*malaco-* + Gr. *sarx* flesh] loss of muscular tissue.
cosis (mal'ah-ko'sis) malacia.
osteon (mal'ah-kos'te-on) [*malaco-* + Gr. *osteon* bone] malacia.
otic (mal'ah-kot'ik) inclined to malacia; soft; said of bone.
tic (mah-lak'tik) 1. softening; emollient. 2. an emollient agent.
die (mal'ah-de') [Fr.] a disease. **m. bleue**, morbus caeruleus. **m. de Capdepont**, dentinogenesis imperfecta. **m. jambes** (da-zhamb'), a disease of rice growers in Louisiana, probably beriberi. **m. de Nicolas et Favre**, lymphogranulovenereum. **m. de plongeurs** (duh-plon-zher'), inflammation and ulceration in divers in the Mediterranean caused by stings of sea anemones. **m. de Roger**, Roger's disease. **du sommeil** (du-so-ma'e), African trypanosomiasis. **m. tics**, Gilles de la Tourette syndrome.
justment (mal'ad-just'ment) in psychiatry, defective adaptation to environment, marked by anxiety, depression, and instability.
y (mal'ah-de) [Fr. *maladie*] any disease or illness.
ma (mah-lag'mah) [Gr.] an emollient or cataplasm.
ma (mal-az') [Fr.] a vague feeling of bodily discomfort.
oplakia (mal'ah-ko-pla'ke-ah) malacoplakia.
gnment (mal'ah-lin'ment) displacement out of line, especially displacement of the teeth from their normal relation to the arch of the dental arch.
nement (mal'ah-lin'ment) malalignment.
(ma'lar) [L. *mala* cheek] pertaining to the cheek or cheek

a (mah-la're-ah) [It. "bad air"] an infectious febrile disease caused by protozoa of the genus *Plasmodium*, which are present in the red blood cells, and are transmitted by the bites of infected mosquitoes of the genus *Anopheles*. The disease is characterized by attacks of chills, fever, and sweating, occurring in cycles which depend on the time required for development of a generation of parasites in the body. After recovery from one attack, the disease has a tendency to become chronic, with occasional relapses. **algid m.**, falciparum malaria characterized by peripheral vascular failure, with coldness of the skin, and extensive involvement of the vessels of the intestinal tract and other abdominal viscera. **benign m.**, vivax m. **bilious remittent m.**, a pernicious form of falciparum malaria characterized by severe nausea, vomiting, high remittent fever, and jaundice appearing the second day after onset. **bovine m.**, Texas fever. **al m.**, falciparum malaria with delirium or coma, as a result of localization of parasites (parasitic thrombus) in the brain. **algid m.**, **m. comato'sa**, cerebral malaria characterized by coma. **dysenteric m.**, falciparum malaria characterized by bloody diarrhea. **estivoautumnal m.**, former name of falciparum malaria when it was endemic in the United States. **falciparum m.**, the most serious form of malaria, caused by *Plasmodium falciparum*, characterized by severe constitutional symptoms and sometimes causing death. **gastric m.**, a form of malaria in which there is continual vomiting. **hepatic m.**, blackwater fever. **hemorrhagic m.**, falciparum malaria in which hemorrhage is a prominent symptom. **hypnotic m.**, malaria that is purposely produced by introduction of malarial parasites, as sometimes used in treating neurosis. **malignant tertian m.**, falciparum m. **ovale m.**, a disease caused by infection with *Plasmodium ovale*, usually characterized by a few regularly recurring tertian febrile paroxysms beginning with a feeling of chilliness or cold shivers rather than rigors typical of vivax malaria, and tending to end in a complete recovery. **pernicious m.**, falciparum m. **tertian m.**, that in which the febrile paroxysms occur every 72 hours, every fourth day counting the day of occurrence as the first day of the cycle; it is caused by *Plasmodium malariae*, which has a 72-hour cycle for completion of each asexual cycle in the red blood cells. **quotidian m.**, that in which the febrile paroxysms occur daily, due to simultaneous infection with two broods of *Plasmodium vivax*, which complete their 42- to 47-hour cycle on alternate days. See *vivax m.* **subtertian m.**, falciparum m. **tertian m.**, that in which the febrile paroxysms occur every 42 hours, or every third day counting the day of occurrence as the first day of the cycle. See *vivax m.* **therapeutic m.**, induced malaria. **vivax m.**, malaria caused by *Plasmodium vivax*, the most common and most likely to recur; the febrile

paroxysms commonly occur every other day (tertian m.), but may occur daily (quotidian m.), if there are two broods of parasites segmenting on alternate days.
malariacidal (mah-la're-ah-si'dal) destructive to malarial plasmodia; plasmodicidal.
malarial (mah-la're-al) pertaining or due to malaria.
malariatherapy (mah-la're-ah-ther'ah-pe) malariotherapy.
malariologist (mah-la're-ol'o-jist) a person versed in or engaged in the study of malaria.
malariology (mah-la're-ol'o-je) [*malaria* + *-logy*] the study of malaria.
malariometry (mah-la're-om'e-tre) the employment of quantitative methods in the study of malaria.
malariotherapy (mah-la're-ol'o-ther'ah-pe) treatment of dementia paralytica by infecting the patient with malarial parasites, usually the parasite of tertian malaria (*Plasmodium vivax*) or of quartan malaria (*P. malariae*).
malarious (mah-la're-us) pertaining to or marked by the presence of malaria.
malaris (mah-la'ris) [L.] malar.
Malassez's disease, rests (mal'ah-saz') [Louis Charles Malassez, physiologist in Paris, 1842-1909] see under *disease* and *rest*.
Malassezia (mal'ah-se'ze-ah) [Louis Charles Malassez] *Pityrosporon orbiculare*.
malassimilation (mal'ah-sim'i-la'shun) [L. *malus* ill + *assimilatio* a rendering like] 1. imperfect, faulty, or disordered assimilation. 2. the inability of the gastrointestinal tract to transport to the body fluids one or more ingested nutrients, whether due to faulty digestion (maldigestion) or to impaired intestinal mucosal transport (malabsorption).
malate (ma'lāt) any salt of malic acid; in biochemistry, the term is often used interchangeably with malic acid (see under *acid*).
malathion (mal'ah-thi'on) chemical name: O,O-dimethyl-S-(1,2-dicarboxyethyl)dithiophosphate. An organophosphorus compound used as an insecticide.
malaxate (mal'ak-sāt) to knead, as in making pills.
malaxation (mal'ak-sa'shun) [Gr. *malaxis* a softening] an act of kneading.
Malcotran (mal'ko-tran) trademark for a preparation of homatropine methylbromide.
maldevelopment (mal'de-vel'op-ment) abnormal growth or development.
maldigestion (mal'di-jes'chun) impaired digestion.
male (māl) 1. an organism of the sex that begets young or that produces spermatozoa. 2. masculine.
maleate (mal'e-āt) any salt or ester of maleic acid.
malemission (mal'e-mish'un) failure of the semen to be discharged from the urinary meatus in coitus.
Malerba's test (mah-ler'bahz) [Pasquale Malerba, Italian physician, 1849-1917] see under *tests*.
maleruption (mal'ē-rup'shun) faulty eruption of a tooth, so that it is out of its normal position.
malethamer (mal-eth'ah-mer) a high weight copolymer of ethylene with maleic anhydride, cross-linked with 1 to 2 per cent, by weight, of vinyl crotonate; an antiperistaltic agent.
malformation (mal'for-ma'shun) [L. *malus* evil + *formatio* a forming] defective or abnormal formation; deformity; an anatomical aberration, especially one acquired during development. **Arnold-Chiari m.**, see under *deformity*.
malfunction (mal-funk'shun) dysfunction.
Malgaigne's amputation, etc. (mal-gānz') [Joseph François Malgaigne, French surgeon, 1806-1865] see under *amputation*, *hook*, *luxation*, *pad*, and *triangle*.
maliasmus (mal'e-as'mus) glanders, or farcy.
malignancy (mah-lig'nān-se) [L. *malignare* to act maliciously] a tendency to progress in virulence; the quality of being malignant.
malignant (mah-lig'nant) [L. *malignans* acting maliciously] tending to become progressively worse and to result in death. Having the properties of anaplasia, invasion, and metastasis; said of tumors.
malignin (mah-lig'nin) a protein fragment present in the serum of patients with malignant glial tumors.
malignogram (mah-lig'no-gram) a systematic arrangement of numerical values assigned to the various factors in cases of carcinoma.
mali-mali (mah'le-mah'le) a form of saltatory spasm endemic in the Philippines.
malingerer (mah-ling'ger-er) [Fr. *malinger* sickly] an individual who is guilty of malingering.
malingering (mah-ling'ger-ing) the willful, deliberate, and

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**The Library of Congress Cataloged the First Issue
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Dorland's illustrated medical dictionary. [1st]—ed.

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illus. (part col.) 23—25 cm.

Title varies: 1st—22d ed., The American illustrated medical dictionary.

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|---------------------------|-------------------------------------|
| I. Medicine—Dictionaries. | I. Dorland, William Alexander |
| Newman, 1864—1956. | II. Title: The American illustrated |
| medical dictionary. | medical dictionary. |

R121.D73 610.3 0-6383 rev 4*

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Japanese (25th Edition)—Hirokawa Publishing Company, Tokyo, Japan

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